mmol/l; 68·5±19·8 mg/100 ml) ($P<0·001$) but not on the test day (maximal increase 1·3±1·1 mmol/l; 23·4±19·8 mg/100 ml). Throughout the remainder of the study period blood glucose was significantly lower on the test day than on the control day, although after lunch it increased by similar increments on the two days. The average blood glucose value during the eight hours was significantly lower on the test day than on the control day (11·2±1·6 mmol/l (202·0±28·8 mg/100 ml) compared with 14·8±1·2 mmol/l (267·0±21·6 mg/100 ml)) ($P<0·001$). Qualitatively similar effects were seen in each patient studied, regardless of the order of treatment. Although none of the patients had symptoms of hypoglycaemia during the study, in two cases values of 2·8 mmol/l (50·5 mg/100 ml) were recorded towards the end of the test day.

Blood lactate concentrations tended to be lower throughout the test day than the control day, significant differences in peak values being recorded after breakfast and lunch (figure). The profile of mean blood pyruvate values was similar to that of lactate values (figure), although none of the differences between values on the control and test days reached significance ($P>0·05$). No consistent changes were seen in the lactate to pyruvate ratio or in the mean blood concentrations of 3-hydroxybutyrate, glycerol, or alanine.

Discussion

Our results show that the α-glucosidehydrolase inhibitor acarbose may greatly decrease the blood glucose concentration in insulin-treated diabetics, particularly after breakfast. This is presumably due to a reduction in the rate of absorption of glucose from the intestinal tract, although we cannot say whether this in turn is due solely to a prolongation of the time taken for carbohydrate to be absorbed or whether there is also a reduction in the total amount absorbed. In normal people the addition of 200 mg acarbose to a 100 g oral load of sucrose causes 40% of the sucrose to pass unabsorbed through the small intestine.[4] A comparable degree of carbohydrate malabsorption is to be expected in diabetics. The subsequent fermentation of non-absorbed sugars by colonic bacteria leads to flatulence, which is a common and often unacceptable side effect of acarbose. The effects of the drug on blood lactate and pyruvate concentrations are less readily explained but may be due to a reduction in the rate of supply of glucose to the glycolytic pathway.

Other methods of slowing carbohydrate absorption in diabetics include adding the non-absorbable carbohydrate guar gum to food.[6,7] Guar is thought to exert its effect mainly by delaying gastric empyting and thus has a different mode of action from that of acarbose. Acarbose has the important advantage that it may be taken as tablets with ordinary food. It remains to be seen whether a suitable treatment regimen can be devised for its use in the long-term management of insulin-dependent diabetes.

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Diet, sunlight, and 25-hydroxy vitamin D in healthy children and adults

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Summary and conclusions

In 110 white West Midlands children serum 25-hydroxy vitamin D (25-OHD) concentrations showed a pronounced seasonal variation, the values being highest in August and lowest in February. The concentrations correlated significantly both with recorded sunlight and with seasonal ultraviolet energy of the sunlight. Children who had had a seaside holiday the previous summer had a higher mean 25-OHD concentration than those who had not had a summer holiday away from home. Correlation between vitamin D intake and serum 25-OHD concentration was not significant.

In February 1977 serum 25-hydroxycholecalciferol and 25-hydroxyergocalciferol concentrations were measured in 11 healthy adults in Cambridge. The mean serum concentration of 25-hydroxycholecalciferol was higher than that of 25-hydroxyergocalciferol. After 5 μg ergocalciferol daily for 28 days the mean serum concentration of 25-hydroxyergocalciferol was significantly increased but still lower than the 25-hydroxycholecalciferol value.

The studies provide further evidence that even in winter serum 25-OHD values in normal people are determined more by previous exposure to summer sunlight than by dietary intake of vitamin D.

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Introduction

Vitamin D is derived by man both from food and from ultraviolet irradiation of 7-dehydrocholesterol in the skin. In the early 1920s Chick in Vienna showed that either oral cod-liver oil or exposure to summer sunlight would prevent and cure rickets in infants.[1] At that time the relative importance of the two sources of calciferol in maintaining normal vitamin D nutrition was not clear. Now, however, we can measure the main circulating metabolite of vitamin D (25-hydroxy vitamin D; 25-OHD) and separate it into 25-hydroxyergocalciferol derived solely from the diet and 25-hydroxycholecalciferol either derived from the diet

or synthetised in the skin.[2] In the following two studies we tried to find the relation in healthy children and adults between diet, light exposure, and serum 25-OHD concentrations.

Subjects and methods

Child study—All the children were seen between October 1974 and March 1976 as part of a wider survey of nutrition in healthy children in Dudley, West Midlands.[3] The purposes of the survey were explained to parents, and the children included in this study were only those whose parents gave permission for venepuncture. Each child was bled once on the day of survey and serum calcium, phosphate, alkaline phosphatase, and 25-OHD values recorded. Intake of vitamin D was calculated from detailed 24-hour dietary recall and use of food tables.[4] Each mother was asked whether her child ate eggs and whether he or she was receiving regularly any proprietary preparation containing vitamin D. Weekly records of the hours of sunshine were obtained from Edgbaston Observatory, about 10 miles (16 km) from where the children lived. Seasonal ultraviolet radiation for sunlight of wavelength 305 nm (in the D-synthetising part of the spectrum) was derived from the tables of Johnson *et al.*[5]

Adult study—Normal healthy adults in the Cambridge area took 5 μg ergocalciferol for 28 days from mid-February 1977. They were chosen because they ate little margarine (the only ergocalciferol-containing food eaten regularly by British adults) and were asked to avoid oily fish and pharmaceutical preparations containing vitamin D for the period of study. Each subject kept a daily record of foods eaten containing vitamin D, and vitamin D intake was calculated from food tables.[4]

Estimation of 25-OHD—Serum 25-OHD concentrations in the children were estimated by competitive protein-binding assay.[6] Separation of 25-OHD into 25-hydroxyergocalciferol and 25-hydroxycholecalciferol was carried out as described.[2]

Results

CHILD STUDY

Serum 25-OHD concentrations were measured in 110 children (51 boys and 59 girls) aged 4·3-6·4 years (mean 5·1±SD 0·5 years). The mean concentration was 41·0±SD 15·5 nmol/l (16·4±6·2 ng/ml), range of 16·0-92·8 nmol/l (6·4-37·1 ng/ml). There was no significant difference in concentrations between boys and girls. No child had clinical or biochemical evidence of rickets. Figure 1 shows the distribution of serum 25-OHD concentrations according to the date on which each blood sample was collected. There was a pronounced seasonal variation in concentrations, the values being highest in late summer and lowest in late winter. Multiple regression analysis showed a highly significant relation between serum 25-OHD values and a sine wave of cycle length 365 days, with a wave peak at 53·0 nmol/l (21·2 ng/ml) in mid-August and a trough at 27·8 nmol/l (11·1 ng/ml) in mid-February ($r = 0{\cdot}67$; $P < 0{\cdot}001$).

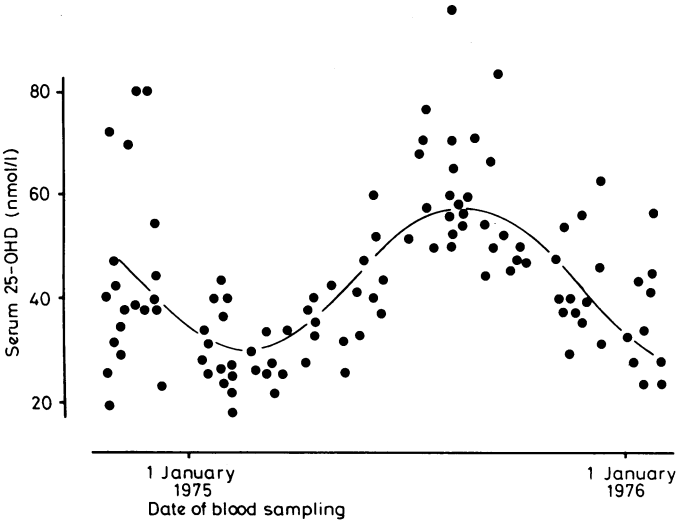

FIG 1—Serum 25-OHD concentrations in all 110 children plotted against date of blood sampling showing best correlation between values and sine wave of cycle length 365 days.
Conversion: SI to traditional units—Serum 25-OHD: 1 nmol/l ≈ 0·4 ng/ml.

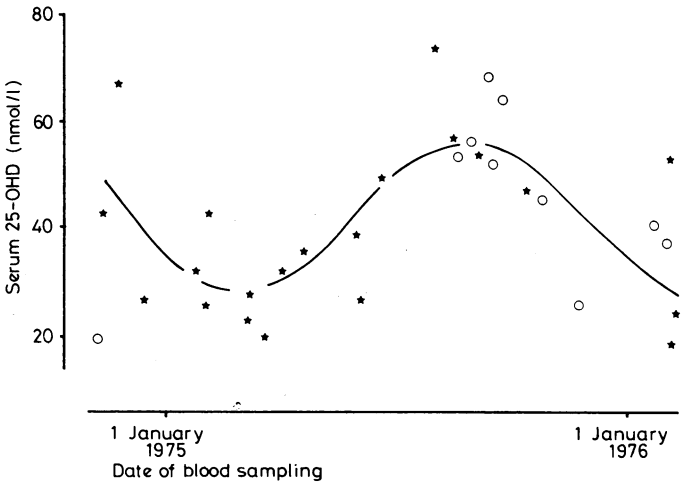

FIG 2—Serum 25-OHD concentrations in 21 children taking proprietary vitamin-D-containing preparations regularly (★) and 10 children who did not eat eggs (○) plotted against best-fit sine wave for all 110 children.
Conversion: SI to traditional units—Serum 25-OHD: 1 nmol/l ≈ 0·4 ng/ml.

Vitamin D intake—Mean vitamin D intake estimated by 24-hour dietary recall was 1·7 μg/day (69 IU) for boys and 1·0 μg/day (40 IU) for girls. In 97 children the intake was below the recommended 2·5 μg/day,[7] 74 children having intakes of less than half this. Serum 25-OHD concentration did not correlate significantly with dietary intake of vitamin D in the previous 24 hours even when allowance was made for seasonal variations in vitamin D values. Figure 2 shows the distribution of 25-OHD concentrations in 21 children who received vitamin-D-containing proprietary preparations daily and 10 children who did not eat eggs. Serum 25-OHD values in these two groups were not significantly different for the time of year from those of the rest of the children.

Light exposure—Table I shows the coefficients of correlation between serum 25-OHD concentrations and log values of recorded hours of sunshine and between 25-OHD concentrations and log values of ultraviolet energy of the sunlight totalled over 1, 4, 6, 8, and 10 weeks before blood sampling. Correlation was highest with log hours of sunshine recorded over the six weeks before blood sampling.

Maximum values for weekly hours of sunshine and ultraviolet light intensity of the sunshine occurred in the first week of July, which was about six weeks before serum 25-OHD concentrations reached their maximum. Concentrations of 25-OHD began to fall when sunlight was about 30 hours a week and ultraviolet light energy 884 J/m²/nm. These values were much higher than when 25-OHD concentrations began to rise in February (about 12 hours of sunshine a week; ultraviolet light energy 44 J/m²/nm). Serum 25-OHD concentrations were higher in children who had had a seaside holiday in the year before blood sampling than in those who had not had a holiday away from home that year (mean difference 8·0 nmol/l (3·2 ng/ml)—$t = 2{\cdot}40$; $P < 0{\cdot}05$).

ADULT STUDY

Table II gives the serum 25-hydroxyergocalciferol and 25-hydroxycholecalciferol concentrations in the 11 adults studied. At the beginning of the study the mean concentration of 25-hydroxyergocalciferol was much lower than that of 25-hydroxycholecalciferol. After 5 μg ergocalciferol daily for one month there was a small but

TABLE I—*Coefficients of correlation between serum 25-OHD concentrations and light accumulated over 1, 4, 6, 8, and 10 weeks before blood sampling*

Weeks of accumulated light:	1	4	6	8	10
Correlation with log hours of sunlight	0·47	0·56	0·61	0·61	0·60
Correlation with log ultraviolet light energy	0·45	0·51	0·53	0·55	0·55

For values over 0·311 $P < 0{\cdot}001$.

TABLE II—*Serum 25-hydroxyergocalciferol and 25-hydroxycholecalciferol concentrations in 11 adults before and after taking 5 μg ergocalciferol daily for 28 days from mid-February 1977**

Subject	Serum 25-hydroxyergocalciferol (nmol/l)		Serum 25-hydroxycholecalciferol (nmol/l)		Mean daily cholecalciferol intake during study (μg)
	Day 0	Day 28	Day 0	Day 28	
1	3·8	7·8	16·5	16·5	3·0
2	10·0	9·0	10·3	9·5	1·6
3	5·3	8·3	14·3	17·3	2·1
4	9·0	10·3	16·8	17·0	0·4
5	4·8	3·8	12·0	11·5	0·8
6	4·5	14·5	13·0	10·0	1·2
7	5·5	12·8	31·3	26·8	1·9
8	5·8	11·5	91·5	47·8	1·7
9	11·0	12·3	20·5	20·0	0·7
10	7·5	15·8	26·5	21·8	3·7
11	4·0	4·8	16·3	12·0	1·6
Mean ± SD	6·5 ± 2·5†	10·0 ± 3·8†	24·5 ± 23·0	19·0 ± 11·0	1·7 ± 1·0

*Mean total serum 25-hydroxycalciferol concentration in these 11 adults in September was 55·8 ± SD 21·3 nmol/l (22·3 ± 8·5 ng/ml).
†Paired *t* test: $P<0.01$. Geometric mean increase of 54% over initial 25-hydroxyergocalciferol concentration.
Conversion: SI to traditional units—Serum 25-hydroxycholecalciferol and 25-hydroxyergocalciferol: 1 nmol/l ≈ 0·4 ng/ml.

significant increase in 25-hydroxyergocalciferol. Correlation between each subject's intake of cholecalciferol during the study and the serum 25-hydroxycholecalciferol concentration was not significant.

Discussion

Variation in circulating 25-OHD is usually attributed to seasonal changes in the ultraviolet energy of sunlight in northern latitudes.[8 9] Thus it is not surprising that we discovered a highly significant correlation between serum 25-OHD concentrations in the children and the ultraviolet energy of the sunlight at the time of blood sampling. The finding that correlations between accumulated sunlight and circulating 25-OHD are greater than those between accumulated ultraviolet energy of the sunlight and 25-OHD concentrations probably indicates that children are most likely to be out of doors, exposed to vitamin-D synthetising ultraviolet light when the sun is shining. Similarly, children who had a seaside holiday were more likely to have had prolonged and extensive exposure to sun, and therefore ultraviolet light, than children who spent the summer in their home town. This would explain the higher mean concentrations of 25-OHD in the children who had a seaside holiday.

The delay between maximum values of light intensity and of serum 25-OHD suggests a prolonged life for 25-OHD or its precursor cholecalciferol in the body. Is there evidence of physiological control of circulating 25-OHD? When serum concentrations of 25-OHD are rising synthesis or mobilisation of 25-OHD or both must be greater than storage or utilisation or both. When concentrations are falling utilisation and/or storage of 25-OHD must exceed synthesis and/or mobilisation from stores. If the synthesis of cholecalciferol, production of circulating 25-OHD, and ultraviolet irradiation of the skin had a simple linear relation then the serum 25-OHD concentration should begin to fall only when ultraviolet light energy falls below the level at which serum 25-OHD begins to increase in the spring. In our group of children, however, serum 25-OHD values were falling long before sunlight or ultraviolet energy had declined to this level. Thus either synthesis of 25-OHD was decreased or storage or utilisation of 25-OHD was increased at higher serum concentrations of 25-OHD. Since 25-hydroxylation of calciferol may be inhibited by serum 25-OHD[10] cholecalciferol might remain bound in skin or other tissues when circulating 25-OHD values are high. The effects of a sunny summer holiday could then remain "stored" as cholecalciferol until falling concentrations of serum 25-OHD in the blood allowed mobilisation and hydroxylation of cholecalciferol. Certainly the body appears to control hydroxylation of cholecalciferol synthetised in the skin, since hypercalcaemia does not result from excessive sunbathing by normal people, although this is a recognised hazard of a high oral vitamin D intake.[11]

In contrast to the effect of sunlight dietary vitamin D apparently has little effect on circulating 25-OHD in either children or adults. Vitamin D intake for each child in the 24 hours before blood sampling was perhaps unlikely to correlate closely with serum 25-OHD values since 24-hour dietary recall is not an accurate method of determining a person's diet.[12] Furthermore, serum 25-OHD may take weeks or months to equilibrate with a constant oral vitamin D intake.[13] Nevertheless, those children who regularly took vitamin-D-containing preparations probably had greater than average vitamin D intakes. In contrast, children who did not eat eggs probably had smaller than average vitamin D intakes, since eggs were the only substantial source of vitamin D[14] eaten regularly by the children. Yet neither of these groups of children had serum 25-OHD values significantly different from those expected for the time of year.

Dietary vitamin D, at least in the form of ergocalciferol, is also relatively unimportant in maintaining circulating 25-OHD in normal adults. Vitamin D intake over a month for each adult did not correlate significantly with his serum 25-OHD value. Daily ingestion of 5 μg ergocalciferol caused a significant increase in 25-hydroxyergocalciferol, although at the end of the month the total serum 25-hydroxyergocalciferol was only just greater than the concentration of total 25-OHD seen in osteomalacia.[15]

Studies both in North America[2] and in the United Kingdom,[15] have shown that the dominant circulating form of serum 25-OHD is usually 25-hydroxycholecalciferol. As in our study, serum 25-hydroxycholecalciferol concentrations correlated more closely with sunlight exposure—or lack of it—than with dietary vitamin D. Thus there is much evidence that even in winter the concentration of circulating 25-OHD in normal people is determined largely by exposure to solar radiation the previous summer and by the rate of utilisation of cholecalciferol and 25-hydroxycholecalciferol stores built up at that time. Such a view must be relevant to understanding the pathogenesis of diseases of which inadequate dietary calciferol is held as the cause.

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